Is appendicectomy associated with an increased risk of cancer? A systematic review and meta-analysis of epidemiological studies

Peter Bannister[a], Mais Tattan[a], Lewis Isaacs[a], Charlie Welch[b], Imogen Rogers[a], Anjum Memon[a]

[a]Department of Primary Care and Public Health, Brighton and Sussex Medical School, UK
[b]Department of Health Sciences, University of York, UK

Background
Dysbiosis of the gut microbiome has been associated with increased risk of luminal and systematic diseases (e.g. inflammatory bowel disease, diabetes) and cancer. The appendix plays an important role in maintaining the gut microbiome, and both appendicitis and appendicectomy are associated with dysbiosis. Given the high rate of appendicectomy in the general population, even a small increase in cancer risk would be of great importance. We conducted a systematic review and meta-analysis of observational epidemiological studies to examine the association between appendicectomy and subsequent development of cancer.

Methods
The Medline, Embase and Web of Science databases were searched to identify eligible studies. Articles were screened by 2 reviewers and included if they reported the risk of any cancer in patients who had undergone appendicectomy. Relevant odds ratio/risk ratio (OR/RR) estimates and corresponding 95% confidence intervals (95% CI) were extracted and a pooled RR for each cancer was calculated using random effects meta-analyses. The protocol was registered with PROSPERO (CRD42020183262).

Results
The literature search identified 3,459 publications; of these 35 studies (26 case-control, 9 cohort) including 35,561 cancer patients were included. The random effects meta-analysis – based on 6 case-control and 2 cohort studies including 1,580 patients – showed that appendicectomy was associated with a borderline increased risk of Hodgkin's lymphoma (pooled RR = 1.15, 95% CI: 1.01 to 1.30). There was no association with any other type of cancer examined (i.e. non-Hodgkin's lymphoma, colorectal, prostate, ovarian, pancreatic).

Conclusion
This meta-analysis showed that appendicectomy may be associated with a somewhat increased risk of developing Hodgkin's lymphoma, and is not associated with the risk of other cancers. Further research is needed to understand the functions of the appendix and biological mechanism of the proposed association between dysbiosis and cancer.

Impact statement
The biological mechanisms behind appendicitis, dysbiosis and subsequent development of cancer need further investigation.

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